

PATENT ABSTRACTS OF JAPAN

(11)Publication number : 2000-109892

(43)Date of publication of application : 18.04.2000

(51)Int.Cl.

C11D 3/386

A61L 2/18

C11D 3/18

C11D 3/48

G02C 13/00

(21)Application number : 10-281035

(71)Applicant : ROHTO PHARMACEUT CO LTD

(22)Date of filing : 02.10.1998

(72)Inventor : KOIKE TETSUHISA

MIWA YUKA

ARITA HARUMASA

(54) POLYSACCHARIDE-CONTAINING LIQUID AGENT FOR CONTACT LENS

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain a liquid agent which combines a high detergent effect and safety, by blending a protease and/or a lipase with chondroitin sulfate and/or hyaluronic acid or a salt thereof.

SOLUTION: The protease and the lipase are each blended usually in an amount of 0.001-10 wt. %. The content of chondroitin sulfate and/or hyaluronic acid or a salt thereof is preferably 0.001-10 wt. %. Chondroitin sulfate and/or hyaluronic acid preferably has a molecular weight of five millions or less. This liquid agent may further contain a fungicide, a surface active agent, a polyol and the like. The fungicide is preferably a polyhexamethylene biguanide, a salt thereof or α -4-[1-tris(2-hydroxyethyl)ammonium chloride-2-butenyl]poly[1-dimethylammonium chloride-2-butenyl]- ω -tris(2-hydroxyethyl)ammonium chloride.

LEGAL STATUS

[Date of request for examination]

22.03.2004

[Date of sending the examiner's decision of rejection]

[Kind of final disposal of application other than withdrawal the examiner's decision of rejection or application converted registration]

[Date of final disposal for application] 01.08.2005

[Patent number]

[Date of registration]

[Number of appeal against examiner's
decision of rejection]

[Date of requesting appeal against examiner's
decision of rejection]

[Date of extinction of right]

Copyright (C); 1998,2003 Japan Patent Office

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

CLAIMS

[Claim(s)]

[Claim 1] Liquids and solutions for contact lenses containing a proteolytic enzyme and/or stearolytic enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts.

[Claim 2] Liquids and solutions according to claim 1 or 2 chondroitin sulfate and/or hyaluronic acid, or those concentration of whose are 0.01 - 1 % of the weight.

[Claim 3] Liquids and solutions according to claim 1 or 2 which furthermore also contain a germicide.

[Claim 4] Liquids and solutions according to claim 3 whose germicide is a polyhexamethylene biguanide, its salt, or an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride.

[Claim 5] Liquids and solutions according to claim 4 whose concentration of a polyhexamethylene biguanide, its salt, or an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride is 0.00001 - 0.1%.

[Claim 6] Liquids and solutions also containing 1 or the matter beyond it furthermore chosen from a nonionic surfactant, an amphoteric surface active agent, an anionic detergent, and a chelating agent according to claim 1.

[Claim 7] Liquids and solutions according to claim 1 which furthermore also contain a glycerol, propylene glycol, or a polyethylene glycol.

[Claim 8] Liquids and solutions according to claim 1 to 7 which are what a contact lens rubs and is used for washing or soak cleaning.

[Translation done.]

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the liquids and solutions which have the detergency which was excellent to the contact lens especially the soft contact lens, or the oxygen permeability hard lens.

[0002]

[Description of the Prior Art] Although a contact lens is a medical supply inserted in a direct eye, adhesion of the dirt of the living body origins, such as protein, a lipid, and mineral salt, is not avoided by the wearing. Moreover, since a contact lens is dealt with with a finger, many adhesion of pollutants from the outside of the body, such as cosmetics, a hand cream, and hair spray, is also seen. If these dirt is left, the permeability of a lens falls and it is hard coming to be visible, and the fall of oxygen permeability may take place, and it may shorten the life of a contact lens, and a feeling of wearing not only gets worse, but it may do a bad influence to eyes, such as an infectious disease, further. Although a contact lens is divided roughly into a hard lens and a soft contact lens, since dirt tends to adhere from the property of a material, in order to harness the outstanding property, removal of a pollutant is important for especially the good hard lens and good water nature soft contact lens of oxygen permeability that were developed aiming at the feeling of wearing superior to recent years. In order to remove the dirt of the adhering protein or a fat, there is a method of using a proteolytic enzyme and stearylolytic enzyme, and care supplies, such as a penetrant remover agent containing these enzymes, are already put in practical use. Usually, in order to wash a contact lens with such enzyme content liquids and solutions, it rubs, washes and carries out in liquid, or enzyme liquid is diluted suitably, and the approach immersed into a diluent is taken.

[0003]

[Problem(s) to be Solved by the Invention] However, importance was attached to rubbing and saving an unstable enzyme stably in water in the case of the enzyme content liquids and solutions for washing, and there was a possibility that the cleaning effect of about [that sufficient detergency is not obtained] and an enzyme might fall. Then, although addition of physical washing by multiple use of a powerful surfactant, an abrasive material, etc. might be achieved in order to compensate sufficient cleaning effect, it was not necessarily desirable in respect of safety. On the other hand, to the dirt which has fixed in the case of the enzyme content liquids and solutions for soak cleaning, the top whose cleaning effect is not enough, since the dilution ratio was not exact, dispersion was in the cleaning effect.

[0004]

[Means for Solving the Problem] this invention persons completed header this invention for the liquids and solutions for contact lenses which suited the above-mentioned purpose and which have a high cleaning effect and high safety being obtained by making a proteolytic enzyme and/or stearylolytic enzyme, and a polysaccharide of a certain kind contain together, as a result of a cleaning effect's repeating research wholeheartedly for the purpose of offering the safe high enzyme content liquids and solutions for contact lenses. That is, this invention offers the liquids and solutions for contact lenses

containing a proteolytic enzyme and/or stearylolytic enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts.

[0005] Polysaccharides, such as chondroitin sulfate and hyaluronic acid, are also the components in tear fluid, and the disinfectant for contact lenses and the preservative for contact lenses containing these are known (JP,63-59960,A, JP,8-253419,A). however, it is indicated by JP,63-59960,A that sodium chondroitin sulfate prevents adsorption on the contact lens of a germicide component, and moreover controls physical-properties change of a contact lens -- **** -- it does not pass and JP,8-253419,A is related with the liquids and solutions for contact lenses useful to prevention of the HIV infection containing a chondroitin sulfate. Before this invention, it was not known for the reasons of that the mucopolysaccharide is mentioned as a component in the tear fluid leading to lens dirt, there being no cleaning effect in itself at all that a mucopolysaccharide is useful as a component of the high liquids and solutions for contact lenses of a cleaning effect.

[0006] this invention persons completed header this invention for a specific mucopolysaccharide reinforcing a cleaning effect. Thus, this invention is based on unexpected knowledge although there is no cleaning effect in itself, that chondroitin sulfate and/or hyaluronic acid have the effectiveness which reinforces the cleaning effect of a proteolytic enzyme or stearylolytic enzyme. Although the cause of such an enhancing effect is not yet solved, the enzyme reaction to this pollutant is promoted, or it is considered by when the negative charge of the front face of chondroitin sulfate and/or hyaluronic acid makes easy to separate, for example the pollutant which has positive charge to the Lords, such as a lysozyme on the front face of a lens, that it is in making it easy to happen.

[0007]

[Embodiment of the Invention] The liquids and solutions for contact lenses of this invention can be used as washing of a contact lens, and preservation liquid. A contact lens rubs one embodiment of this invention, it is the liquids and solutions for washing, and other embodiments are the liquids and solutions for soak cleaning of a contact lens. The liquids and solutions of this invention which rubs and contains an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts on the occasion of implementation of washing are washed [apply them directly, rub them and] and used as a contact lens. Moreover, the soak cleaning liquids and solutions which dilute the liquids and solutions containing the enzyme of this invention with the liquids and solutions containing chondroitin sulfate and/or hyaluronic acid, or those salts, and are obtained in order to carry out soak cleaning, The soak cleaning liquids and solutions used without containing an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts, and diluting, and suitable for the soak cleaning liquids and solutions which dilute the liquids and solutions containing an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts with a physiological saline etc., and are obtained in a contact lens -- time amount immersion is carried out. However, this invention is not limited to the above-mentioned mode, and includes the liquids and solutions for contact lenses of the gestalt of arbitration a condition [containing an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts]. Moreover, the liquids and solutions of this invention have high safety, it is useful also not only as washing but contact lens preservation liquid, and they are liquids and solutions for contact lenses which have an extensive application.

[0008] The liquids and solutions of this invention approve in ophthalmology, and can be made to contain the proteolytic enzyme and/or stearylolytic enzyme of useful arbitration in decomposition removal of the pollutant of a contact lens. A proteolytic enzyme is divided roughly into four kinds, a serine protease, metal protease, a thiol protease, and carboxyl protease, by the active site. In this invention, the serine protease which Bacillus produces is used most effectively. There are specifically a "clear lens pro" (Novo Noldo SUKUBA Io made in industry Japan, Inc.), "BIOPURAZE" (the Nagase Brothers Seikagaku, Inc. make), "alkaline protease" (consonance enzyme company make), "a protease N "Amano" etc." (the Amano Pharmaceuticals incorporated company make), etc., and it can be used, choosing suitably from them. The lipase of an Aspergillus, Streptomyces, and the Bacillus origin is mentioned as stearylolytic enzyme. When using liquids and solutions as it is, that what is necessary is just to choose the suitable range according to the washing capacity of the enzyme to be used in any [in the case of diluting and using it] case, this contractor can choose it as arbitration and can carry out

concentration of the enzyme in liquids and solutions. However, both a proteolytic enzyme and stearolytic enzyme are usually blended at 0.001 - 10% of the weight of a rate. Desirable concentration is 0.01 - 10 % of the weight. When a cleaning effect is not enough if lower than this concentration, and concentration is high, there is a problem in respect of safety. Moreover, in diluting and using the liquids and solutions containing an enzyme, enzyme content liquids and solutions are dropped at 1-several drops and the liquids and solutions for dilution, and it usually dilutes to about 20 to 100 times. For that, the contact lens preservation case currently generally used can be used. For example, the soak cleaning liquids and solutions diluted moderately are obtained by dropping optimum dose ON ** and 1-several drops of enzyme liquids and solutions for the liquids and solutions for dilution at the case for preservation.

[0009] The liquids and solutions of this invention contain chondroitin sulfate **** hyaluronic acid or those salts. As a salt, metal salts, such as sodium salt and potassium salt, etc. are illustrated. These can come to hand as a commercial item from Seikagaku etc. The content in chondroitin sulfate and/or hyaluronic acid, or the liquids and solutions for contact lenses of those salts is 0.001% - 10% preferably, and is desirable. [especially 0.01 - 1% of] Moreover, although millions of things exist in chondroitin sulfate and/or hyaluronic acid from 10,000 molecular weight, if molecular weight is too high, in order to check washing on the contrary according to viscosity, a with a molecular weight of 5 million or less thing is desirable. Especially a desirable thing is a thing with 10,000-3 million molecular weight.

[0010] Moreover, the liquids and solutions of this invention can be made to contain other components, such as a germicide, a surfactant, and polyhydric alcohol. If bacteria adhere and propagate at a contact lens, the liquids and solutions with which the cause of the infectious disease of an eye contains a germicide from things to the prevention are useful. Especially in the case of a water nature contact lens, since it is easy to increase bacteria, daily sterilization disinfection is required. Therefore, although the liquids and solutions which can perform washing and sterilization were desirable, since a germicide checked the cleaning effect of an enzyme, it was difficult to obtain conventionally the liquids and solutions which can perform washing and sterilization to coincidence. However, since the cleaning effect is reinforced as shown in the below-mentioned example of a trial, even if the liquids and solutions containing the chondroitin sulfate and/or the hyaluronic acid, or those salts of this invention blend an enzyme together with a germicide, they can demonstrate sufficient cleaning effect, and its usefulness is high. Therefore, this invention offers the liquids and solutions for contact lenses also containing a germicide again. As an example of a germicide, there is a germicide called quarternary ammonium salt, such as biguanides, such as oxidizing agents, such as a hydrogen peroxide, and chlorhexidine, a polyhexamethylene biguanide or its salt, and an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride. Desirable germicides are a polyhexamethylene biguanide or its salt, and an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride. 0.00001% - 0.1% of the concentration of the germicide to blend is desirable, and is more desirable so that the washing activity of an enzyme may not be checked with a high-concentration germicide. [0.00001% - 0.05% of] Moreover, in the case of a polyhexamethylene biguanide or its salt, especially desirable concentration is 0.00001 - 0.001%, and, in the case of quarternary ammonium salt, such as an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride, is 0.0001 - 0.01%. A commercial item can be suitably used for these germicides.

[0011] Furthermore, if an anionic detergent, an amphoteric surface active agent, or a nonionic surfactant is blended with the liquids and solutions of this invention, a cleaning effect can be reinforced further. The concentration in the liquids and solutions (it is mixed liquor when diluting) applied to a contact lens is desirable, and the loadings of a surfactant are range which becomes 0.1 - 5% preferably especially 0.01 to 10%. The enzyme stabilization effect or detergency which are expected when concentration is too low are not obtained, but when concentration is too high, there is a danger of producing a dermatopathy.

[0012] As an anionic detergent, there are alkyl sulfate, a polyoxyethylene-alkyl-ether sulfate, N-

acylamino acid chloride, polyoxyethylene-alkyl-ether acetate, alkyl sulfo carboxylate, alpha-olefin sulfonate, polyoxyethylene-alkyl-ether phosphate, etc. As an amphoteric surface active agent, there are an alkyl dimethylamino acetic-acid betaine, a fatty-acid amide propyl dimethylamino acetic-acid betaine, alkylpolyamino ethylglycine, etc. As a nonionic surfactant, ~~polyoxyethylene polyoxy PUROPUREN~~ alkyl ether, A sorbitan fatty acid ester, ~~guru~~ serine fatty acid ester, polyglyceryl fatty acid ester, Polyoxyethylene sorbitan fatty acid ester, polyoxyethylene sorbitol fatty acid ester, Polyoxyethylene glycerine fatty acid ester, a polyethylene glycol, There are polyoxyethylene alkyl ether, polyoxyethylene alkyl phenyl ether, polyoxyethylene hydrogenated castor oil, polyoxyethylene alkylamine, polyoxyethylene fatty acid amide, etc.

[0013] Moreover, a cleaning effect can be heightened by carrying out business also of the metal chelating agent to the liquids and solutions of this invention. As a metal chelating agent, edetic acid, the edetate (the disodium edetate, the edetate calckum disodium, edetate trisodium, edetic acid 4 sodium), etc. are illustrated. As an example of a metal chelating agent, ethylenediaminetetraacetic acid, nitrilotriacetic acid, and its salt can be mentioned, in mixed liquor, 0.01% - 1% is desirable especially desirable, and the content is 0.05% - 0.5%.

[0014] Furthermore, enzyme stability can be further raised by blending polyhydric alcohol with the liquids and solutions of this invention. As an example of polyhydric alcohol, a glycerol, a diethylene glycol, propylene glycol, a polyethylene glycol, a sorbitol, etc. are mentioned. Especially desirable polyhydric alcohol is a glycerol, a polyethylene glycol, or propylene glycol excellent not only in stabilization of an enzyme but the cleaning effect of lipid dirt. It is effective to blend into mixed liquor in the amount which polyhydric alcohol contains at 0.5 - 4.0% of a rate. Polyhydric-alcohol concentration may affect the physical properties of a contact lens at 4.0% or more.

[0015] Buffers, such as the buffer usually used by the technical field concerned, for example, a boric acid system, a phosphoric-acid system, a carbonic acid system, a citric-acid system, a tartaric-acid system, a lactic-acid system, an acetic-acid system, and a phthalic-acid system, can be used for the liquids and solutions of this invention. In the liquids and solutions of this invention, a boric-acid system or a phosphoric-acid system buffer is desirable, and a boric-acid system has it from stabilization of an enzyme, or the field of enhancement of sterilizing properties. [more desirable] Moreover, the concentration of a buffer can be blended 0.01 to 20% that what is necessary is just the concentration which maintains an enzyme at stability. At 0.01% or less, the stability of the buffer force and an enzyme may become low, and it may have a bad influence on the physical properties of a contact lens by concentration higher than 20%.

[0016] The liquids and solutions for contact lenses of this invention are useful as a cleaning agent and a preservative, it is desirable that pH is usually 4-9, and it is desirable that it is especially pH 6-8. Moreover, unless the cleaning effect of this invention liquids and solutions is spoiled, a need component well-known in addition to the component of the above-mentioned publication at the technical fields concerned, such as antiseptics, pH regulator, an isotonizing agent, a surfactant, amino acid, a preservative, and mineral, can be blended suitably. As antiseptics, a sorbic acid, sorbic acid potassium salt, p-hydroxybenzoic esters, chlorhexidine glyconate, a benzalkonium chloride, benzethonium chloride, etc. are mentioned. As a pH regulator, a glycerol, grape sugar, a mannitol, etc. are mentioned as isotonizing agents, such as a hydrochloric acid, an acetic acid, and a sodium hydroxide. Although an example is given to below and this invention is explained to it, this invention is not limited to these.

[0017] Examples 1-6 [Table 1]

(単位 : w/v%)

実施例番号	1	2	3	4	5	6
蛋白分解酵素 (クリアレンス [®] プロ)	0.4	0.2				
蛋白分解酵素 (アルカリ リポテアーゼ GL-440)			0.2	0.05	0.05	0.05
脂肪分解酵素 (クリアレンス [®] リボ)		0.2	0.2		0.2	0.2
コントロールイン硫酸Na	0.5	0.1		0.05	0.05	
ポリヘキサメチレン ビクアミド塩酸塩				0.0001		
ヒアルロン酸Na			0.05			0.05
グリセリン	2.0		2.0	2.0	2.0	2.0
プロピレングリコール		2.0				
ポリオキシエチレンポリオキシ プロピレングリコール	0.1	0.1	0.1	0.1	0.1	0.1
ホウ酸	1.5	0.2	0.2	1.5	0.2	0.2
ホウ砂	3.5	0.7	0.7	3.5	0.7	0.7
エデト酸2ナトリウム	0.2	0.05	0.05	0.2	0.05	0.05

The component of each formula of a publication is mixed to Table 1, and liquids and solutions are prepared. The liquids and solutions of examples 1-6 can be rubbed, and can be used as liquids and solutions for washing. Moreover, the liquids and solutions of examples 1-3 can be suitably diluted with the liquid for dilution, such as a physiological saline, and it can consider as the liquids and solutions for immersion. The liquids and solutions of each example added, adjusted and ** (ed) purified water.
[0018] Examples 7-18 [Table 2]

(単位 : w/v%)

液剤	A	B	C	D	E	F	G
液の種類	酵素	酵素	酵素	希釈	希釈	希釈	希釈
蛋白分解酵素 (ブロナーゼN)		0.8					
蛋白分解酵素 (アムリブ ロアゼ GL-440)	4.5		4.5				
脂肪分解酵素 (クリアズ 賦)			0.2				
コト ロイソ酵素 Na					0.5	0.1	0.05
ホ リヘキサチレンヒ グ アニト 塩酸塩						0.0001	
ヒアルロン酸 Na				0.25			0.05
塩化ナトリウム				0.7	0.7	0.7	0.7
塩化カリウム				0.1	0.1	0.1	0.1
リン酸 2水素カリウム				0.02	0.02		
リン酸 2水素 2ナトリウム・12水和物				0.3	0.3		
グリセリン	32.8		35.0				
ブ ペン グ リ コ ル		33.5					
ボ リ オ キ シ ジ ェ ン ボ リ オ キ シ ブ ペ ン グ リ コ ル				0.1	0.1	0.1	0.1
ホウ酸						0.02	0.15
ホウ砂						0.005	0.015
エド 酸 2 ナトリウム				0.05	0.05	0.05	0.05

The enzyme content liquids and solutions A, B, and C of a publication and the liquids and solutions D, E, F, and G for dilution containing polysaccharide are separately prepared to Table 2, respectively. The liquids and solutions for soak cleaning are obtained combining these enzyme liquid and a diluent to arbitration. Each liquids and solutions were adjusted and ** (ed) with purified water.

[0019] Example 1 of a trial The test fluid which diluted and obtained the enzyme liquid A of a publication 25 times with Diluent E to the cleaning effect test report 2 of liquids and solutions, and the comparison liquid which diluted enzyme liquid A with liquid excluding sodium chondroitin sulfate from Diluent E similarly, and obtained it with it were used. 1.0g of ovalbumins, 0.1g of lysozyme chloride, and 0.1g of pig stomach mucin were measured, artificial tear fluid was dissolved in the 100ml phosphate buffer, it created as pH=7.2, intact contact lens ** (braces Ore TM Toray Industries, Inc. make) or contact lens ** (1 day AKYU view TM made in Johnson & Johnson) was immersed in 5ml of this liquid, and it shook at 37 degrees C for about 8 hours. It is a physiological saline, the superfluous artificial tear fluid of lens ** was rinsed, and it was immersed into the lens case (the Ginza plan company make) with test fluid or 1.5ml of comparison liquid, and it boiled with the sterilizer (the Ginza plan company make), and was immersed further for about 15 hours. It exchanged for new liquid and this actuation was repeated 3 times. In lens **, it is a physiological saline, superfluous artificial tear fluid was rinsed, and it was immersed in the lens case (the Ginza plan company make) with test fluid or 1.5ml of comparison liquid for about 15 hours. It exchanged for new test fluid, this actuation was repeated 3 times, and after being eating raw food finally and rinsing, the condition of a lens was observed visually.

A result is shown in Table 3.

[Table 3]

	試験液	比較液
レンズ①	◎	○
レンズ②	○	△

Evaluation: There is almost no dirt known by O viewing.

O The dirt known visually remains a little.

The dirt known by ** viewing remains considerably.

The result of Table 3 shows that the cleaning effect of the liquids and solutions of this invention is high.

[Translation done.]

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.*** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

TECHNICAL FIELD

[Field of the Invention] This invention relates to the liquids and solutions which have the detergency which was excellent to the contact lens especially the soft contact lens, or the oxygen permeability hard lens.

[Translation done.]

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

PRIOR ART

[Description of the Prior Art] Although a contact lens is a medical supply inserted in a direct eye, adhesion of the dirt of the living body origins, such as protein, a lipid, and mineral salt, is not avoided by the wearing. Moreover, since a contact lens is dealt with with a finger, many adhesion of pollutants from the outside of the body, such as cosmetics, a hand cream, and hair spray, is also seen. If these dirt is left, the permeability of a lens falls and it is hard coming to be visible, and the fall of oxygen permeability may take place, and it may shorten the life of a contact lens, and a feeling of wearing not only gets worse, but it may do a bad influence to eyes, such as an infectious disease, further. Although a contact lens is divided roughly into a hard lens and a soft contact lens, since dirt tends to adhere from the property of a material, in order to harness the outstanding property, removal of a pollutant is important for especially the good hard lens and good water nature soft contact lens of oxygen permeability that were developed aiming at the feeling of wearing superior to recent years. In order to remove the dirt of the adhering protein or a fat, there is a method of using a proteolytic enzyme and stearylolytic enzyme, and care supplies, such as a penetrant remover agent containing these enzymes, are already put in practical use. Usually, in order to wash a contact lens with such enzyme content liquids and solutions, it rubs, washes and carries out in liquid, or enzyme liquid is diluted suitably, and the approach immersed into a diluent is taken.

[Translation done.]

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] However, importance was attached to rubbing and saving an unstable enzyme stably in water in the case of the enzyme content liquids and solutions for washing, and there was a possibility that the cleaning effect of about [that sufficient detergency is not obtained] and an enzyme might fall. Then, although addition of physical washing by multiple use of a powerful surfactant, an abrasive material, etc. might be achieved in order to compensate sufficient cleaning effect, it was not necessarily desirable in respect of safety. On the other hand, to the dirt which has fixed in the case of the enzyme content liquids and solutions for soak cleaning, the top whose cleaning effect is not enough, since the dilution ratio was not exact, dispersion was in the cleaning effect.

[Translation done.]

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

MEANS

[Means for Solving the Problem] this invention persons completed header this invention for the liquids and solutions for contact lenses which suited the above-mentioned purpose and which have a high cleaning effect and high safety being obtained by making a proteolytic enzyme and/or stearylolytic enzyme, and a polysaccharide of a certain kind contain together, as a result of a cleaning effect's repeating research wholeheartedly for the purpose of offering the safe high enzyme content liquids and solutions for contact lenses. That is, this invention offers the liquids and solutions for contact lenses containing a proteolytic enzyme and/or stearylolytic enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts.

[0005] Polysaccharides, such as chondroitin sulfate and hyaluronic acid, are also the components in tear fluid, and the disinfectant for contact lenses and the preservative for contact lenses containing these are known (JP,63-59960,A, JP,8-253419,A). however, it is indicated by JP,63-59960,A that sodium chondroitin sulfate prevents adsorption on the contact lens of a germicide component, and moreover controls physical-properties change of a contact lens -- **** -- it does not pass and JP,8-253419,A is related with the liquids and solutions for contact lenses useful to prevention of the HIV infection containing a chondroitin sulfate. Before this invention, it was not known for the reasons of that the mucopolysaccharide is mentioned as a component in the tear fluid leading to lens dirt, there being no cleaning effect in itself at all that a mucopolysaccharide is useful as a component of the high liquids and solutions for contact lenses of a cleaning effect.

[0006] this invention persons completed header this invention for a specific mucopolysaccharide reinforcing a cleaning effect. Thus, this invention is based on unexpected knowledge although there is no cleaning effect in itself, that chondroitin sulfate and/or hyaluronic acid have the effectiveness which reinforces the cleaning effect of a proteolytic enzyme or stearylolytic enzyme. Although the cause of such an enhancing effect is not yet solved, the enzyme reaction to this pollutant is promoted, or it is considered by when the negative charge of the front face of chondroitin sulfate and/or hyaluronic acid makes easy to separate, for example the pollutant which has positive charge to the Lords, such as a lysozyme on the front face of a lens, that it is in making it easy to happen.

[0007]

[Embodiment of the Invention] The liquids and solutions for contact lenses of this invention can be used as washing of a contact lens, and preservation liquid. A contact lens rubs one embodiment of this invention, it is the liquids and solutions for washing, and other embodiments are the liquids and solutions for soak cleaning of a contact lens. The liquids and solutions of this invention which rubs and contains an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts on the occasion of implementation of washing are washed [apply them directly, rub them and] and used as a contact lens. Moreover, the soak cleaning liquids and solutions which dilute the liquids and solutions containing the enzyme of this invention with the liquids and solutions containing chondroitin sulfate and/or hyaluronic acid, or those salts, and are obtained in order to carry out soak cleaning, The soak cleaning liquids and solutions used without containing an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts, and diluting, and suitable for the soak cleaning liquids and solutions which dilute the liquids and

solutions containing an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts with a physiological saline etc., and are obtained in a contact lens -- time amount immersion is carried out. However, this invention is not limited to the above-mentioned mode, and includes the liquids and solutions for contact lenses of the gestalt of arbitration a condition [containing an enzyme, chondroitin sulfate and/or hyaluronic acid, or those salts]. Moreover, the liquids and solutions of this invention have high safety, it is useful also not only as washing but contact lens preservation liquid, and they are liquids and solutions for contact lenses which have an extensive application.

[0008] The liquids and solutions of this invention approve in ophthalmology, and can be made to contain the proteolytic enzyme and/or stearylolytic enzyme of useful arbitration in decomposition removal of the pollutant of a contact lens. A proteolytic enzyme is divided roughly into four kinds, a serine protease, metal protease, a thiol protease, and carboxyl protease, by the active site. In this invention, the serine protease which Bacillus produces is used most effectively. There are specifically a "clear lens pro" (Novo Noldo SUKUBA Io made in industry Japan, Inc.), "BIOPURAZE" (the Nagase Brothers Seikagaku, Inc. make), "alkaline protease" (consonance enzyme company make), "a protease N "Amano" etc." (the Amano Pharmaceuticals incorporated company make), etc., and it can be used, choosing suitably from them. The lipase of an Aspergillus, Streptomyces, and the Bacillus origin is mentioned as stearylolytic enzyme. When using liquids and solutions as it is, that what is necessary is just to choose the suitable range according to the washing capacity of the enzyme to be used in any [in the case of diluting and using it] case, this contractor can choose it as arbitration and can carry out concentration of the enzyme in liquids and solutions. However, both a proteolytic enzyme and stearylolytic enzyme are usually blended at 0.001 - 10% of the weight of a rate. Desirable concentration is 0.01 - 10 % of the weight. When a cleaning effect is not enough if lower than this concentration, and concentration is high, there is a problem in respect of safety. Moreover, in diluting and using the liquids and solutions containing an enzyme, enzyme content liquids and solutions are dropped at 1-several drops and the liquids and solutions for dilution, and it usually dilutes to about 20 to 100 times. For that, the contact lens preservation case currently generally used can be used. For example, the soak cleaning liquids and solutions diluted moderately are obtained by dropping optimum dose ON ** and 1-several drops of enzyme liquids and solutions for the liquids and solutions for dilution at the case for preservation.

[0009] The liquids and solutions of this invention contain chondroitin sulfate **** hyaluronic acid or those salts. As a salt, metal salts, such as sodium salt and potassium salt, etc. are illustrated. These can come to hand as a commercial item from Seikagaku etc. The content in chondroitin sulfate and/or hyaluronic acid, or the liquids and solutions for contact lenses of those salts is 0.001% - 10% preferably, and is desirable. [especially 0.01 - 1% of] Moreover, although millions of things exist in chondroitin sulfate and/or hyaluronic acid from 10,000 molecular weight, if molecular weight is too high, in order to check washing on the contrary according to viscosity, a with a molecular weight of 5 million or less thing is desirable. Especially a desirable thing is a thing with 10,000-3 million molecular weight.

[0010] Moreover, the liquids and solutions of this invention can be made to contain other components, such as a germicide, a surfactant, and polyhydric alcohol. If bacteria adhere and propagate at a contact lens, the liquids and solutions with which the cause of the infectious disease of an eye contains a germicide from things to the prevention are useful. Especially in the case of a water nature contact lens, since it is easy to increase bacteria, daily sterilization disinfection is required. Therefore, although the liquids and solutions which can perform washing and sterilization were desirable, since a germicide checked the cleaning effect of an enzyme, it was difficult to obtain conventionally the liquids and solutions which can perform washing and sterilization to coincidence. However, since the cleaning effect is reinforced as shown in the below-mentioned example of a trial, even if the liquids and solutions containing the chondroitin sulfate and/or the hyaluronic acid, or those salts of this invention blend an enzyme together with a germicide, they can demonstrate sufficient cleaning effect, and its usefulness is high. Therefore, this invention offers the liquids and solutions for contact lenses also containing a germicide again. As an example of a germicide, there is a germicide called quarternary ammonium salt, such as biguanides, such as oxidizing agents, such as a hydrogen peroxide, and chlorhexidine, a

polyhexamethylene biguanide or its salt, and an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride. Desirable germicides are, a polyhexamethylene biguanide or its salt, and an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride. 0.00001% - 0.1% of the concentration of the germicide to blend is desirable, and is more desirable so that the washing activity of an enzyme may not be checked with a high-concentration germicide. [0.00001% - 0.05% of] Moreover, in the case of a polyhexamethylene biguanide or its salt, especially desirable concentration is 0.00001 - 0.001%, and, in the case of quarternary ammonium salt, such as an alpha-4-[1-tris (2-hydroxyethyl) ammonium-chloride-2-butenyl] Pori [1-dimethyl ammonium-chloride-2-butenyl]-omega-tris (2-hydroxyethyl) ammonium chloride, is 0.0001 - 0.01%. A commercial item can be suitably used for these germicides. [0011] Furthermore, if an anionic detergent, an amphoteric surface active agent, or a nonionic surfactant is blended with the liquids and solutions of this invention, a cleaning effect can be reinforced further. The concentration in the liquids and solutions (it is mixed liquor when diluting) applied to a contact lens is desirable, and the loadings of a surfactant are range which becomes 0.1 - 5% preferably especially 0.01 to 10%. The enzyme stabilization effect or detergency which are expected when concentration is too low are not obtained, but when concentration is too high, there is a danger of producing a dermatopathy.

[0012] As an anionic detergent, there are alkyl sulfate, a polyoxyethylene-alkyl-ether sulfate, N-acylamino acid chloride, polyoxyethylene-alkyl-ether acetate, alkyl sulfo carboxylate, alpha-olefin sulfonate, polyoxyethylene-alkyl-ether phosphate, etc. As an amphoteric surface active agent, there are an alkyl dimethylamino acetic-acid betaine, a fatty-acid amide propyl dimethylamino acetic-acid betaine, alkylpolyamino ethylglycine, etc. As a nonionic surfactant, polyoxyethylene polyoxy PUROPUREN alkyl ether, A sorbitan fatty acid ester, guru serine fatty acid ester, polyglyceryl fatty acid ester, Polyoxyethylene sorbitan fatty acid ester, polyoxyethylene sorbitol fatty acid ester, Polyoxyethylene glycerine fatty acid ester, a polyethylene glycol, There are polyoxyethylene alkyl ether, polyoxyethylene alkyl phenyl ether, polyoxyethylene hydrogenated castor oil, polyoxyethylene alkylamine, polyoxyethylene fatty acid amide, etc.

[0013] Moreover, a cleaning effect can be heightened by carrying out business also of the metal chelating agent to the liquids and solutions of this invention. As a metal chelating agent, edetic acid, the edetate (the disodium edetate, the edetate calckum disodium, edetate trisodium, edetic acid 4 sodium), etc. are illustrated. As an example of a metal chelating agent, ethylenediaminetetraacetic acid, nitrilotriacetic acid, and its salt can be mentioned, in mixed liquor, 0.01% - 1% is desirable especially desirable, and the content is 0.05% - 0.5%.

[0014] Furthermore, enzyme stability can be further raised by blending polyhydric alcohol with the liquids and solutions of this invention. As an example of polyhydric alcohol, a glycerol, a diethylene glycol, propylene glycol, a polyethylene glycol, a sorbitol, etc. are mentioned. Especially desirable polyhydric alcohol is a glycerol, a polyethylene glycol, or propylene glycol excellent not only in stabilization of an enzyme but the cleaning effect of lipid dirt. It is effective to blend into mixed liquor in the amount which polyhydric alcohol contains at 0.5 - 4.0% of a rate. Polyhydric-alcohol concentration may affect the physical properties of a contact lens at 4.0% or more.

[0015] Buffers, such as the buffer usually used by the technical field concerned, for example, a boric acid system, a phosphoric-acid system, a carbonic acid system, a citric-acid system, a tartaric-acid system, a lactic-acid system, an acetic-acid system, and a phthalic-acid system, can be used for the liquids and solutions of this invention. In the liquids and solutions of this invention, a boric-acid system or a phosphoric-acid system buffer is desirable, and a boric-acid system has it from stabilization of an enzyme, or the field of enhancement of sterilizing properties. [more desirable] Moreover, the concentration of a buffer can be blended 0.01 to 20% that what is necessary is just the concentration which maintains an enzyme at stability. At 0.01% or less, the stability of the buffer force and an enzyme may become low, and it may have a bad influence on the physical properties of a contact lens by concentration higher than 20%.

[0016] The liquids and solutions for contact lenses of this invention are useful as a cleaning agent and a preservative, it is desirable that pH is usually 4-9, and it is desirable that it is especially pH 6-8. Moreover, unless the cleaning effect of this invention liquids and solutions is spoiled, a need component well-known in addition to the component of the above-mentioned publication at the technical fields concerned, such as antiseptics, pH regulator, an isotonizing agent, a surfactant, amino acid, a preservative, and mineral, can be blended suitably. As antiseptics, a sorbic acid, sorbic acid potassium salt, p-hydroxybenzoic esters, chlorhexidine glyconate, a benzalkonium chloride, benzethonium chloride, etc. are mentioned. As a pH regulator, a glycerol, grape sugar, a mannitol, etc. are mentioned as isotonizing agents, such as a hydrochloric acid, an acetic acid, and a sodium hydroxide. Although an example is given to below and this invention is explained to it, this invention is not limited to these.

[0017] Examples 1-6 [Table 1]

(単位 : w/v%)

実施例番号	1	2	3	4	5	6
蛋白分解酵素 (クリアレンス [®] プロ)	0.4	0.2				
蛋白分解酵素(アルカリ プロテアーゼ [®] GL-440)			0.2	0.05	0.05	0.05
脂肪分解酵素 (クリアレンス [®] リボ)		0.2	0.2		0.2	0.2
コント [®] ロイチン硫酸Na	0.5	0.1		0.05	0.05	
ボ [®] リヘキサメチレン ピク [®] アニト [®] 塩酸塩				0.0001		
ヒアルロン酸Na			0.05			0.05
グリセリン	2.0		2.0	2.0	2.0	2.0
プロピレングリコール		2.0				
ボ [®] リオキシエチレンボ [®] リオキシ プロピレングリコール	0.1	0.1	0.1	0.1	0.1	0.1
ホウ酸	1.5	0.2	0.2	1.5	0.2	0.2
ホウ砂	3.5	0.7	0.7	3.5	0.7	0.7
エデ [®] ト酸2ナトリウム	0.2	0.05	0.05	0.2	0.05	0.05

The component of each formula of a publication is mixed to Table 1, and liquids and solutions are prepared. The liquids and solutions of examples 1-6 can be rubbed, and can be used as liquids and solutions for washing. Moreover, the liquids and solutions of examples 1-3 can be suitably diluted with the liquid for dilution, such as a physiological saline, and it can consider as the liquids and solutions for immersion. The liquids and solutions of each example added, adjusted and ^{**}(ed) purified water.

[0018] Examples 7-18 [Table 2]

(単位: $\text{w/v}\%$)

液剤	A	B	C	D	E	F	G
液の種類	酵素	酵素	酵素	希釈	希釈	希釈	希釈
蛋白分解酵素 (プロテアーゼ)		0.8					
蛋白分解酵素 (アルカリプロテアーゼ GL-440)	4.5		4.5				
脂肪分解酵素 (クリスタリブ)			0.2				
コト・ロイソチン酸 Na					0.5	0.1	0.05
ポリヘキサメチレンビ グアノール 塩酸塩						0.0001	
ヒアルロン酸 Na				0.25			0.05
塩化ナトリウム				0.7	0.7	0.7	0.7
塩化カリウム				0.1	0.1	0.1	0.1
リン酸二水素ナトリウム				0.02	0.02		
リン酸二水素ナトリウム・12水和物				0.3	0.3		
グリセリン	32.8		35.0				
プロピレングリコール		33.5					
ポリオキシエチレンポリ オキシプロピレングリ コール				0.1	0.1	0.1	0.1
ホウ酸						0.02	0.15
ホウ砂						0.005	0.015
エドト酸ナトリウム				0.05	0.05	0.05	0.05

The enzyme content liquids and solutions A, B, and C of a publication and the liquids and solutions D, E, F, and G for dilution containing polysaccharide are separately prepared to Table 2, respectively. The liquids and solutions for soak cleaning are obtained combining these enzyme liquid and a diluent to arbitration. Each liquids and solutions were adjusted and ** (ed) with purified water.

[0019] Example 1 of a trial The test fluid which diluted and obtained the enzyme liquid A of a publication 25 times with Diluent E to the cleaning effect test report 2 of liquids and solutions, and the comparison liquid which diluted enzyme liquid A with liquid excluding sodium chondroitin sulfate from Diluent E similarly, and obtained it with it were used. 1.0g of ovalbumins, 0.1g of lysozyme chloride, and 0.1g of pig stomach mucin were measured, artificial tear fluid was dissolved in the 100ml phosphate buffer, it created as pH=7.2, intact contact lens ** (braces Ore TM Toray Industries, Inc. make) or contact lens ** (1 day AKYU view TM made in Johnson & Johnson) was immersed in 5ml of this liquid, and it shook at 37 degrees C for about 8 hours. It is a physiological saline, the superfluous artificial tear fluid of lens ** was rinsed, and it was immersed into the lens case (the Ginza plan company make) with test fluid or 1.5ml of comparison liquid, and it boiled with the sterilizer (the Ginza plan company make), and was immersed further for about 15 hours. It exchanged for new liquid and this actuation was repeated 3 times. In lens **, it is a physiological saline, superfluous artificial tear fluid was rinsed, and it was immersed in the lens case (the Ginza plan company make) with test fluid or 1.5ml of comparison liquid for about 15 hours. It exchanged for new test fluid, this actuation was repeated 3 times, and after being eating raw food finally and rinsing, the condition of a lens was observed visually.

A result is shown in Table 3.

[Table 3]

	試験液	比較液
レンズ①	◎	○
レンズ②	○	△

Evaluation: There is almost no dirt known by ○ viewing.

○ The dirt known visually remains a little.

The dirt known by ** viewing remains considerably.

The result of Table 3 shows that the cleaning effect of the liquids and solutions of this invention is high.

[Translation done.]